UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,562	01/26/2001	William J. Curatolo	PC9674AJTJ	8513

152 7590 11/09/2009

CHERNOFF, VILHAUER, MCCLUNG & STENZEL, LLP
601 SW Second Avenue
Suite 1600
PORTLAND, OR 97204-3157

EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
11/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/770,562	CURATOLO ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/30/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,23,28-38,49-51 and 53-56* is/are pending in the application.

4a) Of the above claim(s) *28-35 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,23,36,37,49-51 and 53-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. In view of the Appeal Brief filed on 7/30/09, PROSECUTION IS HEREBY REOPENED. New rejections using previously cited art that accounts for claims 50, 51 and 56 are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618.

DETAILED ACTION

The examiner acknowledges receipt Appeal Brief and remarks and change of address/power of attorney all filed 04/16/09. Claims 1, 4, 23, 28-38, 49-51 and 53-56 remain pending.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1, 4, 49-51 and 53-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyajima et al. (EP 0 344 603).

4. Claim 1 is a composition comprising solid dispersion; the solid dispersion consists of sparingly water-soluble drug and hydroxypropyl methylcellulose acetate succinate (HPMCAS); the drug is molecularly dispersed and amorphous; the drug to polymer ratio is between 1:0.4 and 1:20. No specific drug is recited except that the drug is sparingly soluble in water.

5. Miyajima describes formulating NZ-105, a dihydropyridine phosphonic acid derivative, drug that is poorly soluble in water (abstract; page 2, lines 14-35; page 3, lines 6-9), by dissolving NZ-105 and HPMCAS in an organic solvent and removing the solvent by vacuum drying, spray drying or freeze drying to yield compositions that are remarkably enhanced bioavailability (page 3, lines 16-20; page 4, lines 56-58) with solid dispersions resulting from spray-drying. 1-7 parts or 3-5 parts by weight of HPMCAS are used per 1 part by weight of NZ-105 so that the ratio of the drug to polymer in Miyajima is 1:1 to 1:7 or 1:3 to 1:5 are species of the broader ration of 1:0.4 to 1:20 and the narrower range or species anticipates the broader range meeting the drug polymer ratio of claims 1, 55 and 56. Claim 51 is a product by process

claim and the claim is thus met by the composition of Miyajima. For claim 1, parts (a) and (b) are the properties of the dosage form. Claim 1 recites spray dried dispersion which in claim 4 is amorphous when undispersed and the recitation in claim 4 is also directed to the properties of the dosage form. "Spray dried" is the process of making the dispersion, however, the product in Miyajima is also spray dried. Claims 4, 49, 53 and 54 recite the properties of the composition so that the composition of Miyajima meets the claims. The solvent is removed by vacuum drying, spray-drying or freeze-drying and the dried product is inherently free of solvent and Miyajima did not say that the product has associated solvent so that claim 50 is met. The particle size of 100-400 or 150-300 mesh of the Miyajima particles encompasses the particles size of 100 micron since 400 and 300 mesh sizes are less than 100 micron.

Response to Arguments

6. Appellant's arguments filed 7/30/2009 have been fully considered but they are not persuasive.

7. Appellant argues that claim 1 comprises spray-dried solid dispersion that consists of poorly water soluble drug and HPMCAS and the drug being molecularly dispersed and amorphous in the dispersion and that the "consists" of language excludes ingredients that are not mentioned except for impurities while Miyajima makes 3- and 4-component compositions and not any two component dispersion of drug and HPMCAS, and the preparation method does not use spray drying.

8. The examiner disagrees with the appellant: a) the comprising language of the claims is open (see line 1 of claim 1) so that even though the second line of the claim uses "consists" of language, the comprising language in line 1 of the claims keeps the composition open. b) While

spray drying is the process of preparing the composition and would not accord patentable weight to compositions except for when the process leads to distinctive structural characteristics to the final product, in the present case, Miyajima prepares the product by dissolving the drug and HPMCAS in an organic solvent and removes the solvent by vacuum drying or spray drying or freeze drying (see page 4, lines 57-59). Thus, Miyajima contemplates spray drying as one of the processes for removing the solvent just as in the claim. Thus the examiner disagrees that Miyajima does not use spray drying.

9. Appellant further argues that Miyajima does not characterize the drug as amorphous or crystalline or mixture amorphous and crystalline in some other state.

10. While the examiner agrees with the appellant that Miyajima did not use any of those terms to describe the drug, amorphous drug composition is prepared by spray drying according to applicant's claims and because Miyajima uses spray drying to obtain the product of drug and polymer, the product formed is a dispersion.

11. Claims 1, 4, 49-51 and 53-56 are rejected under 35 U.S.C. 102(a) as being anticipated by Kigoshi et al. (EP 0 784 974).

12. Kigoshi describes solid dispersions containing xanthine derivatives and polymer (title; abstract; page 2, lines 21, 22, 44, 45); the xanthine derivatives are slightly soluble in water meeting the sparingly water soluble drug of the claims; the polymer can be a cellulose derivative (page 3, line 58) and hydroxypropylmethyl cellulose acetate succinate (HPMCAS) is one the derivatives named (page 4, line 8) meeting the requirements of claim 1. One of the processes of removing the solvent from the formation of the solid dispersion is by spray-dry granulator (page

4, line 38) and the resulting granules/particles are isolated (page 4, lines 49, 50). The ratio of the xanthine derivatives of compound I to the polymer ranges from 3:1 to 1:5 (page 4, lines 12, 13) with the ratio of 1:5 intersecting points within the recited ratio of from 1:0.4 to 1:20 of the claims with the disclosed ratio meeting the requirements of claims 1, 55 and 56. Claim 1 recites spray dried dispersion which in claim 4 is amorphous when undispersed and the recitation in claim 4 is also directed to the properties of the dosage form. Claims 4, 49, 53 and 54 recite the properties of the composition so that the composition of Kigoshi meets the claims. Claim 51 is a product by process claim and the claim is thus met by the composition of Miyajima. Claim 1 recites spray dried dispersion which in claim 4 is amorphous when undispersed and the recitation in claim 4 is also directed to the properties of the dosage form. "Spray dried" is the process of making the dispersion, however, the product in Kigoshi is also spray dried. The solvent is removed by vacuum drying, spray-drying or freeze-drying and the dried product is inherently free of solvent and Kigoshi did not say that the product has associated solvent so that claim 50 is met.

Response to Arguments

13. Appellant's arguments filed 7/30/09 have been fully considered but they are not persuasive.

14. Appellant argues that HPMCAS is one of 22 polymers used by Kigoshi with 15 different process choices and that based on the many polymer and processes used by Kigoshi to making the solid dispersion, the examiner employed hindsight in picking, choosing and combining various portions of the reference and that the portions selected are not stated to be directly related

to each other citing Ex parte Beuther, 71 USPQ2d 1313 and Net MoneyIN inc. v. VeriSign Inc., 88 USPQ2d 1751.

15. The examiner disagrees with the appellant that the polymers are not related. All the polymers contemplated for use in the formation of solid dispersion of drugs in Kigoshi are all polymers that disperse the drugs. Also, different categories of polymers are disclosed and HPMCAS is one of 10 of the cellulose type polymers that form solid dispersion of drugs. Therefore, because, these polymers are all related to each other by the Kigoshi art, it appears the Ex parte Beuther findings support the combination since the finding by the Board in that case was that "portions of the disclosure not directly related to each other by the teachings of the reference" were used. Therefore, no hindsight reasoning was used as it relates to the polymers. With regards to appellant's arguments that15 processes were used in Kigoshi, the examiner notes that, Kigoshi in several sections of the disclosure specifically mentions spray drying as a means of forming the solid dispersion (see for example, page 4, lines 38, 46, 49, 58). It is further noted that all the processes are related to each because all are used to prepare solid dispersions. With regards to Net MoneyIN inc. v. VeriSign Inc., the examiner notes that the issue in that case was an issue of "means plus function language" of the claims and the current claims are not drafted as "means plus function."

16. Claims 1, 4, 49, 53, 54, 55 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 57-176907 (Eng. Translation provided by applicant in 1449 filed 5/07/2001).

17. JP 57-176907 discloses composition comprising AS-56C in substantially amorphous form in one or more bases selected from hydroxypropyl methyl cellulose phthalate, HPMCAS, methyl acrylate-methacrylic acid-methacrylate copolymers and methacrylic acid-methyl

methacrylate copolymers (first full paragraph of page 2); the product is obtained by spray drying (4th full paragraph page 2); the ratio of drug AS-56C to polymer ranges from 1:4, 1:3, 1:2, 1:20 in Examples 1-12. The ratios meet the ratio requirements for the drug to polymer of claims 1, 55 and 56. Claims 4, 49, 53 and 54 recite the properties of the composition so that these claims are met. Since the composition of JP 57-176907 spray dried just as the claimed composition, the composition of the JP 57-176907 is a dispersion and the drug is molecularly dispersed.

18.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 1, 23, 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyajima et al. (EP 0 344 603) or Kigoshi et al. (EP 0 784 974).

21. Miyajima: Miyajima is described above as anticipating claim 1. For claims 50 and 51, since the formulation of Miyajima and that of the instant claims are spray dried, it would be reasonable to expect that the residual solvent in the formulation of Miyajima and the composition of the claims would be the same except where applicant shows that not to be the case. Although, Miyajima's spray dried formulations are granules, Miyajima does not specifically teach the particle size is less than 100 μm in diameter. But, the particle size of 100-400 or 150-300 mesh of the Miyajima particles encompasses the particles size of 100 micron since 400 and

300 mesh size are less than 100 micron. Therefore, the particles of Miyajima at 400 or 300 mesh (37 μm and 53-44 μm). Therefore, taking the teachings of Miyajima, one having ordinary skill in the art at the time the invention was made, would reasonably expect that the particles of the dispersion would have sizes that are less than 100 μm according to the disclosed size of 100-400 and 150-300 mesh (149-37 μm and about 105-44 μm).

22. Kigoshi: Kigoshi has been described above as anticipating claim 1. For claims 50 and 51, since the formulation of Kigoshi and that of the instant claims are spray dried, it would be reasonable to expect that the residual solvent in the formulation of Kigoshi and the composition of the claims would be the same except there is factual evidence that it's not. Although, Kigoshi's spray dried formulations are granules, Kigoshi does not specifically teach the particle size of claim 23. But, in example 1, the particle size is 200 mesh (74 μm) and since other polymers such as the HPMCAS are contemplated (see claims 5 and 6), it is reasonable to expect that when the other polymers such as hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, or carboxymethylethyl cellulose (see claims 5 and 6) are used, the drug and polymer solution when also be sprayed onto a seed of 200 mesh (74 μm) would form dispersed solids having size of 200 mesh (74 μm). Therefore, taking the teachings of Kigoshi, one having ordinary skill in the art at the time the invention was made would reasonably expect that solution of drug and HPMCAS when sprayed onto a core particle having the size of 200 mesh (74 μm) would expectedly result in dispersion of drug and HPMCAS having a size of 74 μm, which is less than 100 μm.

Response to Arguments

23. Appellant's arguments filed 7/30/09 have been fully considered but they are not persuasive.

24. Appellant states that the reasons provided for rejecting claims 23 under 35 USC over Miyajima or Kigoshi falls short of the standard set forth by the KSR court.

25. The examiner disagrees because the particles of Miyajima contain particles that are less than 100 μm as described in the rejection. As for Kigoshi, the particles having the size of 74 μm are less that 100 μm so that using HPMCAS as the polymer, one would expect to form particles having sizes of less than 100 μm by using the teachings of Kigoshi.

26. Claims 1, 4, 36, 37 49-51 and 53-56 rejected under 35 U.S.C. 103(a) as being unpatentable over Kigoshi et al. (EP 0 784 974) in view of Madhusoodanan et al. ("Efficacy of risperidone treatment for psychoses associated with schizophrenia, schizoaffective disorder, bipolar disorder, or senile dementia in 11 geriatric patients: a case series," in J. Clin. Psychiatry, 1995 Nov;56(11):514-8 (Abstract enclosed)) and further in view of Bymaster et al. (US 6,147,072).

27. Kigoshi has been described as teaching the limitations of claim 1 and dependent claims 4, 49-51 and 53-56. The active agents in Kigoshi are xanthine derivatives and these derivatives have anti-dementia activity in addition to diuretic activity, kidney protecting activity and cerebral function-improving activity (page 2, lines 5-8).

28. The xanthine derivatives are not the antipsychotic drugs of claims 36 and 37. But, drugs such as the antipsychotic drug, risperidone is known in the art to have effect on psychosis related to dementia, bipolar disorder and schizophrenia according to the abstract of Madhusoodanan in J.

Clin. Psychiatry, 1995 Nov. Further also, risperidone and ziprasidone are known anti-psychotic drugs (see Bymaster at column 2, lines 22 and 43). One anti-dementia agent can be used in place of the other with the expectation that either will deliver the desired anti-dementia effect.

29. Therefore, taking the teachings of Kigoshi, Madhusoodanan and Bymaster, one having ordinary skill in the art at the time the invention was made would reasonably expect that solid dispersions obtained by substituting ziprasidone for the xanthine derivatives in Kigoshi would have the expected anti-dementia activity in a person in need thereof.

30. No claim is allowed.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

32. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

33. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618

/Blessing M. Fubara/
Examiner, Art Unit 1618